We claim:

1. A compound of the formula

(pyro)Glu-His-V-Ser-W-X-Y-Arg-Pro-Z

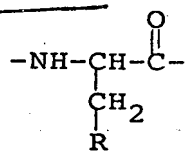
(I)

and the pharmaceutically acceptable salts thereof wherein:

V is tryptophyl, phenylalanyl or 3-(1-naphthyl)-L-alanyl;

W is tyrosyl, phenylalanyl or 3-(1-pentafluorophenyl)-L-alanyl;

X is a D-amino acid residue



wherein R is

(a) a carbocyclic aryl-containing radical selected from the group consisting of naphthyl, anthryl, fluorenyl, phenanthryl, biphenylyl, benzhydryl and phenyl substituted with three or more straight chain lower alkyl groups; or

(b) a saturated carbocyclic radical selected from the group consisting of cyclohexyl substituted with three or more straight chain lower alkyl groups, perhydronaphthyl, perhydrobiphenylyl, perhydro-2,2-diphenylmethyl and adamantyl;

Y is leucyl, isoleucyl, nor-leucyl or N-methylleucyl;

Z is glycinamide or $\frac{1}{m}NH\frac{1}{h_1}R^1$, wherein

R^1 is lower alkyl, cycloalkyl, fluoro lower alkyl or $-NH-\overset{O}{\overset{\|}{C}}-NH-R^2$ wherein R^2 is hydrogen or lower alkyl.

2. The compound of claim 1 wherein V is tryptophyl or phenylalanyl; W is tyrosyl; X is 3-(2-naphthyl)-D-alanyl or 3-(2,4,6-trimethylphenyl)-D-alanyl; Y is leucyl or N-methyl-leucyl; and Z is glycinamide or ~~prolylethylamide~~ prolylethylamide.

3. The compound of claim 2 wherein X is 3-(2-naphthyl)-D-alanyl.

4. The compound of claim 2 which is (pyro)Glu-His-Trp-Ser-Tyr-3-(2-naphthyl)-D-alanyl-Leu-Arg-Pro-Gly-NH_2 and the pharmaceutically acceptable acid salts thereof.

5. The compound of claim 3 which is (pyro)Glu-His-Trp-Ser-Tyr-3-(2-naphthyl)-D-alanyl-N-methyl-Leu-Arg-Pro-Gly-NH_2 and the pharmaceutically acceptable salts thereof.

6. The compound of claim 3 which is (pyro)Glu-His-Trp-Ser-Tyr-3-(2-naphthyl)-D-alanyl-Leu-Arg-Pro-NHEt and the pharmaceutically acceptable salts thereof.

7. The compound of claim 3 which is (pyro)Glu-His-Trp-Ser-Tyr-3-(2-naphthyl)-D-alanyl-N-methyl-Leu-Arg-Pro-NHEt and the pharmaceutically acceptable salts thereof.

8. The compound of Claim 3 which is (pyro)Glu-His-Phe-Ser-Syr-3-(2-naphthyl)-D-alanyl-Leu-Arg-Pro-Gly-NH_2 and the pharmaceuticlly acceptable salts thereof.

9. The compound of Claim 2 wherein X is 3-(2,4,6-trimethylphenyl)-D-alanyl.

10. The compound of Claim 9 which is (pyro)Glu-His-Trp-Ser-Tyr-3-(2,4,6-trimethylphenyl)-D-alanyl-Leu-Arg-Pro-Gly-NH_2 and the pharmaceutically acceptable salts thereof.

11. A method of inhibiting ovulation in a female mammalian subject which method comprises administering to said subject an effective amount of a compound of the formula

(pyro)Glu-His-V-Ser-W-X-Y-Arg-Pro-Z (I)

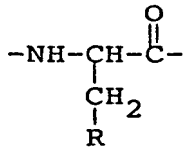
(I)

or a pharmaceutically acceptable salt thereof wherein:

V is tryptophyl, phenylalanyl or 3-(1-naphthyl)-L-alanyl;

W is tyrosyl, phenylalanyl or 3-(1-pentafluorophenyl)-L-alanyl;

X is a D-amino acid residue



wherein R is

(a) a carbocyclic aryl-containing radical selected from the group consisting of naphthyl, anthryl, fluorenyl, phenanthryl, biphenylyl, benzhydryl and phenyl substituted with three or more straight chain lower alkyl groups; or

(b) a saturated carbocyclic radical selected from the group consisting of cyclohexyl substituted with three or more straight chain lower alkyl groups, perhydronaphthyl perhydrobiphenylyl, perhydro-2,2-diphenylmethyl and adamantyl;

Y is leucyl, isoleucyl, nor-leucyl or N-methyl-leucyl;

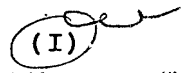
Z is glycinamide or $\frac{l}{m}NH\frac{l}{m}R^1$, wherein

R^1 is lower alkyl, cycloalkyl, fluoro lower alkyl or $-NH-\overset{O}{\overset{\|}{C}}-NH-R^2$ wherein

R^2 is hydrogen or lower alkyl, or a pharmaceutical composition containing same.

12. A pharmaceutical composition ~~for inhibition of ovulation in a female mammal~~ comprising an effective amount of a compound of the formula

(pyro)Glu-His-V-Ser-W-X-Y-Arg-Pro-Z (I)

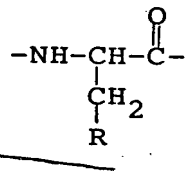


or a pharmaceutically acceptable salt thereof wherein:

V is tryptophyl, phenylalanyl or 3-(1-naphthyl)-L-alanyl;

W is tyrosyl, phenylalanyl or 3-(1-pentafluorophenyl)-L-alanyl;

X is a D-amino acid residue



wherein R is

(a) a carbocyclic aryl-containing radical selected from the group consisting of naphthyl, anthryl, fluorenyl, phenanthryl, biphenylyl, benzhydryl and phenyl substituted with three or more straight chain lower alkyl groups; or

(b) a saturated carbocyclic radical selected from the group consisting of cyclohexyl substituted with three or more straight chain lower alkyl groups, perhydronaphthyl, perhydrobiphenylyl, perhydro-2,2-diphenylmethyl and adamantyl;

Y is leucyl, isoleucyl, nor-leucyl or N-methylleucyl;

Z is glycinamide or $-NH-R^1$, wherein

R^1 is lower alkyl, cycloalkyl, fluoro lower alkyl or $-NH-\overset{O}{\overset{\|}{C}}-NH-R^2$ wherein

R^2 is hydrogen or lower alkyl, in admixture with a pharmaceutically acceptable non-toxic carrier.

13. A method of treating endometriosis in a female mammalian subject which method comprises administering to

said subject an effective amount of a compound of the formula

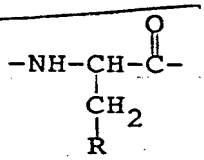
(pyro)Glu-His-V-Ser-W-X-Y-Arg-Pro-Z (I)

or a pharmaceutically acceptable salt thereof wherein:

V is tryptophyl, phenylalanyl or 3-(1-naphthyl)-L-alanyl;

W is tyrosyl, phenylalanyl or 3-(1-pentafluorophenyl)-L-alanyl;

X is a D-amino acid residue



wherein R is

(a) a carbocyclic aryl-containing radical selected from the group consisting of naphthyl, anthryl, fluorenyl, phenanthryl, biphenylyl, benzhydryl and phenyl substituted with three or more straight chain lower alkyl groups; or

(b) a saturated carbocyclic radical selected from the group consisting of cyclohexyl substituted with three or more straight chain lower alkyl groups, perhydronaphthyl, perhydrobiphenylyl, perhydro-2,2-diphenylmethyl and adamantyl;

Y is leucyl, isoleucyl, nor-leucyl or N-methyl-

leucyl;

Z is glycinamide or $-NH-R^1$, wherein

R^1 is lower alkyl, cycloalkyl, fluoro lower alkyl or $-NH-\overset{O}{\overset{\|}{C}}-NH-R^2$ wherein

R^2 is hydrogen or lower alkyl, or a pharmaceutical composition containing same.

14. A pharmaceutical composition for treatment of endometriosis in a female mammal comprising a compound of the formula

(pyro)Glu-His-V-Ser-W-X-Y-Arg-Pro-Z

(I)

or a pharmaceutically acceptable salt thereof wherein:

V is tryptophyl, phenylalanyl or 3-(1-naphthyl)-L-alanyl;

W is tyrosyl, phenylalanyl or 3-(1-pentafluorophenyl)-L-alanyl;

X is a D-amino acid

$$-NH-\underset{\underset{R}{|}}{\overset{\overset{CH_2}{|}}{CH}}-\overset{O}{\overset{\|}{C}}-$$

wherein R is

(a) a carbocyclic aryl-containing radical selected from the group consisting of naphthyl, anthryl, fluorenyl, phenanthryl, biphenylyl, benzhydryl and phenyl substituted with three or more straight chain lower alkyl

groups; or

(b) a saturated carbocyclic radical selected from the group consisting of cyclohexyl substituted with three or more straight chain lower alkyl groups, perhydronaphthyl, perhydrobiphenylyl, perhydro-2,2-diphenylmethyl and adamantyl;

Y is leucyl, isoleucyl, nor-leucyl or N-methyl-leucyl;

Z is glycinamide or $-NH-R^1$, wherein

R^1 is lower alkyl, cycloalkyl, fluoro lower alkyl or $-NH-\overset{O}{\overset{\|}{C}}-NH-R^2$ wherein

R^2 is hydrogen or lower alkyl, in addition with a pharmaceutically acceptable, non-toxic carrier.

14. A method of treating benign prostatic hypertrophy in a male mammalian subject which method comprises administering to said subject an effective amount of a compound of the formula

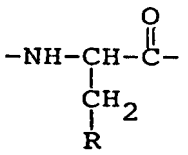
(pyro)Glu-His-V-Ser-W-X-Y-Arg-Pro-Z (I)

or a pharmaceutically acceptable salt thereof wherein:

V is tryptophyl, phenylalanyl or 3-(1-naphthyl)-L-alanyl;

W is tyrosyl, phenylalanyl or 3-(1-pentafluorophenyl)-L-alanyl;

X is a D-amino acid residue



wherein R is

(a) a carbocyclic aryl-containing radical selected from the group consisting of naphthyl, anthryl, fluorenyl, phenanthryl, biphenylyl, benzhydryl and phenyl substituted with three or more straight chain lower alkyl groups; or

(b) a saturated carbocyclic radical selected from the group consisting of cyclohexyl substituted with three or more straight chain lower alkyl groups, perhydronaphthyl, perhydrobiphenylyl, perhydro-2,2-diphenylmethyl and adamantyl;

Y is leucyl, isoleucyl, nor-leucyl or N-methyl-leucyl;

Z is glycinamide or $-NH-R^1$, wherein

R^1 is lower alkyl, cycloalkyl, fluoro lower alkyl or $-NH-\overset{O}{\overset{\|}{C}}-NH-R^2$ wherein

R^2 is hydrogen or lower alkyl, or a pharmaceutical composition containing same.

16. A pharmaceutical composition for treatment of benign prostatic hypertrophy in a male mammal comprising a compound of the formula

(pyro)Glu-His-V-Ser-W-X-Y-Arg-Pro-Z

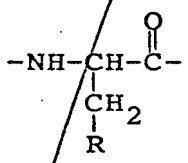
(I)

or a pharmaceutically acceptable salt thereof wherein:

V is tryptophyl, phenylalanyl or 3-(1-naphthyl)-L-alanyl;

W is tyrosyl, phenylalanyl or 3-(1-pentafluorophenyl)-L-alanyl;

X is a D-amino acid



wherein R is

(a) a carbocyclic aryl-containing radical selected from the group consisting of naphthyl, anthryl, fluorenyl, phenanthryl, biphenylyl, benzhydryl and phenyl substituted with three or more straight chain lower alkyl groups; or

(b) a saturated carbocyclic radical selected from the group consisting of cyclohexyl substituted with three or more straight chain lower alkyl groups, perhydronaphthyl, perhydrobiphenylyl, perhydro-2,2-diphenylmethyl and adamantyl;

Y is leucyl, isoleucyl, nor-leucyl or N-methyl-leucyl;

Z is glycinamide or $-NH-R^1$, wherein

R^1 is lower alkyl, cycloalkyl, fluoro lower alkyl or $-NH-\overset{O}{\overset{\|}{C}}-NH-R^2$ wherein

R^2 is hydrogen or lower alkyl, in admixture with a pharmaceutically acceptable, non-toxic carrier.

17. A method of inhibiting spermatogenesis in a male mammalian subject which method comprises

administering to said subject an effective amount of a compound of the formula

(pyro)Glu-His-V-Ser-W-X-Y-Arg-Pro-Z

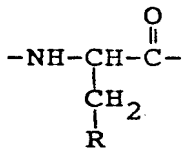
(I)

or a pharmaceutically acceptable salt thereof wherein:

V is tryptophyl, phenylalanyl or 3-(1-naphthyl)-L-alanyl;

W is tyrosyl, phenylalanyl or 3-(1-pentafluorophenyl)-L-alanyl;

X is a D-amino acid residue



wherein R is

(a) a carbocyclic aryl-containing radical selected from the group consisting of naphthyl, anthryl, fluorenyl, phenanthryl, biphenylyl, benzhydryl and phenyl substituted with three or more straight chain lower alkyl groups; or

(b) a saturated carbocyclic radical selected from the group consisting of cyclohexyl substituted with three or more straight chain lower alkyl groups, perhydronaphthyl, perhydrobiphenylyl, perhydro-2,2-diphenylmethyl and adamantyl;

Y is leucyl, isoleucyl, nor-leucyl or N-methylleucyl;

Z is glycinamide or $\overset{1}{\underset{m}{}}NH\text{-}\overset{1}{\underset{n}{}}R^1$, wherein

R^1 is lower alkyl, cycloalkyl, fluoro lower alkyl or $-NH-\overset{O}{\overset{\|}{C}}-NH-R^2$ wherein

R^2 is hydrogen or lower alkyl, or a pharmaceutical composition containing same.

18. A pharmaceutical composition for inhibiting spermatogenesis in a male mammal comprising a compound of the formula

(pyro)Glu-His-V-Ser-W-X-Y-Arg-Pro-Z

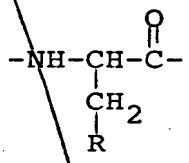
(I)

and the pharmaceutically acceptable salts thereof wherein:

V is tryptophyl, phenylalanyl or 3-(1-naphthyl)-L-alanyl;

W is tyrosyl, phenylalanyl or 3-(1-pentafluorophenyl)-L-alanyl;

X is a D-amino acid



wherein R is

(a) a carbocyclic aryl-containing radical selected from the group consisting of naphthyl, anthryl, fluorenyl, phenanthryl, biphenylyl, benzhydryl and phenyl substituted with three or more straight chain lower alkyl groups; or

(b) a saturated carbocyclic radical selected from the group consisting of cyclohexyl substituted with three or more straight chain lower alkyl groups, perhydro-

naphthyl, perhydrobiphenylyl, perhydro-2,2-diphenylmethyl and adamantyl;

Y is leucyl, isoleucyl, nor-leucyl or N-methyl-leucyl;

Z is glycinamide or $-NH-R^1$, wherein

R^1 is lower alkyl, cycloalkyl, fluoro lower alkyl or $-NH-\overset{O}{\overset{\|}{C}}-NH-R^2$ wherein

R^2 is hydrogen or lower alkyl, in admixture with a pharmaceutically acceptable, non-toxic carrier.

19. A process for the preparation of a compound of the formula

(pyro)Glu-His-V-Ser-W-X-Y-Arg-Pro-Z

(I)

and the pharmaceutically acceptable salts thereof wherein:

V is tryptophyl, phenylalanyl or 3-(1-naphthyl)-L-alanyl;

W is tyrosyl, phenylalanyl or 3-(1-pentafluoro-phenyl)-L-alanyl;

X is a D-amino acid

$$-NH-\underset{\displaystyle CH_2\\ \displaystyle R}{\overset{\displaystyle O}{\overset{\|}{CH}}}-C-$$

wherein R is

(a) a carbocyclic aryl-containing radical selected from the group consisting of naphthyl, anthryl, fluorenyl, phenanthryl, biphenylyl, benzhydryl and phenyl

substituted with three or more straight chain lower alkyl groups; or

(b) a saturated carbocyclic radical selected from the group consisting of cyclohexyl substituted with three or more straight chain lower alkyl groups, perhydronaphthyl, perhydrobiphenylyl, perhydro-2,2-diphenylmethyl and adamantyl;

Y is leucyl, isoleucyl, nor-leucyl or N-methyl-leucyl;

Z is glycinamide or $-NH-R^1$, wherein

R^1 is lower alkyl, cycloalkyl, fluoro lower alkyl or $-NH-\overset{O}{\overset{\|}{C}}-NH-R^2$ wherein

R^2 is hydrogen or lower alkyl, which process comprises:

(i) removing protecting groups and optionally covalently bound solid support from a protected polypeptide to afford a compound of Formula (I) or a salt thereof, and optionally

(ii) converting a compound of Formula (I) to a pharmaceutically acceptable salt,

(iii) converting a salt of a compound of Formula (I) to a pharmaceutically acceptable salt, or

(iv) decomposing a salt of a compound of Formula (I) to a free polypeptide of Formula (I).